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Diagnosing Orthostatic Hypotension – A narrative review of the evidence

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Short title:

Diagnosing orthostatic hypotension

Abstract

Background

Orthostatic hypotension (OH) is very common, particularly in older populations.

Diagnostic criteria exist but appear to be arbitrary rather than evidence-based.

This review will visit the evidence for diagnostic strategies for OH.

Data sources

Medline (OvidSP), EMBASE (OvidSP), ISI Web of Science, the Health Technology Assessments Database and the Cochrane Library.

Areas of agreement

A five-minute rest is required before measuring baseline. An active stand with continuous blood pressure (BP) monitoring is preferable to a tilt-test to identify *initial* OH in particular. At least two-minutes in the upright position is required.

A systolic drop of 20 or a diastolic drop of 10 is supported by the evidence.

Reproducibility when testing for OH is poor.

Areas of controversy

Is the active stand preferable to the tilt-test to diagnose *classical* OH? Although continuous BP monitoring increases diagnostic rates, does it improve clinical outcomes? Should symptoms be used to inform diagnosis?

Areas timely for research

Establishing the long-term clinical outcomes for transient drops in BP detected on continuous, non-invasive monitoring. Evaluating the different patterns of BP drop to aid diagnosis and direct treatment.

Key words: orthostatic hypotension, diagnosis, postural hypotension

Background

Orthostatic hypotension (OH), sometimes known as postural hypotension, occurs when an individual's blood pressure (BP) drops on assuming an upright position. It is highly prevalent, affecting approximately one third of older people living in the community and up to two thirds of people in long-term care ^{1 2}. It can be anticipated that with the expanding older population and longer survival of people with chronic disease the prevalence of OH may increase.

Following the first description of postural hypotension in 1925 there was relatively little progress made on its diagnosis and treatment ³. One of the limiting factors was a wide variation in criteria used for the diagnosis. It was not until over 70 years later in 1996 that an expert working group published the first consensus criteria for the diagnosis of OH ⁴. This enabled some clinical and academic progress to be made but did leave many unanswered questions, particularly with the increasingly widespread use of non-invasive, continuous BP monitoring systems.

Once again, there are now several diagnostic criteria available (see Table 2). These are largely similar but do have some methodological differences, particularly the additional criteria that were added to the consensus criteria in 2011 ². This review will visit and appraise the evidence regarding the methods used to diagnose OH and will make recommendations based on this existing evidence. A summary of the most recent research published since the 2011 consensus is displayed in Table 1.

Search strategy and selection criteria

Medline (OvidSP), EMBASE (OvidSP), ISI Web of Science, the Health Technology Assessments Database and the Cochrane Library were searched for articles written in the English language and published since 1946. Reference lists of identified studies were searched until no additional studies could be found. Search terms used were orthostatic hypotension, postural hypotension, orthostatic syndromes and diagnosis. Articles relating to postural tachycardia, vasovagal syncope and other orthostatic disorders were excluded.

An attempt was made to review studies according to the STARD (Standards for Reporting of Diagnostic Accuracy Studies⁵) criteria, but this was abandoned due to the complete lack of studies reporting in this way.

Results

Current Guidelines

Current guidelines from several different sources are summarised in Table 2.

Establishing a baseline BP

As the postural drop required for a diagnosis of OH is dependent upon the baseline value, it is an essential component of investigation. However, this is not reflected within the literature with very little evidence to inform practice. In 2006, the European Federation of Neurological Sciences (EFNS) made a recommendation for five minutes of supine rest, prior to orthostatic challenge,

based on expert opinion and consensus ⁶. Where evidence does exist, it is from small studies of limited methodological value, but their results generally support the EFNS recommendation.

Several strategies have been used to determine the optimal baseline BP, with variable methods of BP measurement, different timings of BP measurement and various resting conditions. One of the earlier studies, using intermittent sphygmomanometry, was a retrospective review of the BP readings from 300 people in 1989 during a senior's health screening programme. Readings were taken at five, seven and nine minutes of baseline rest, in the supine position. The BP at the seventh minute was significantly lower than that at five minutes, but did not differ statistically to the BP at nine minutes. The researchers then studied a small prospective group (50 individuals from a geriatric medicine clinic) to determine whether it was the frequency of BP measurement, or the duration of supine rest that led to the reduction in BP. This prospective group underwent a 10-minute supine rest with BP measurement at five, seven and nine minutes and then a 10-minute rest with BP measurement once at nine minutes (further details of the protocol are not described). The BP was significantly higher at nine minutes when measured as a single reading than when measured in a series of BP measurements. The authors therefore concluded that it is the effect of acclimatising to repeated BP measurement which results in BP decline, rather than the duration of the rest period⁷.

This theory is not supported by the more recent studies using non-invasive, continuous BP measurement. A study involving 17 healthy controls (70-84

years), 18 ambulatory people with diastolic heart failure (aged 70-80) and 24 hospitalised patients (aged 69-98) with co-morbidity aimed to determine how long would be required to achieve stable baseline BP values⁸. Systolic BP did not change significantly in any of the groups over 10 minutes of supine rest, but diastolic BP did decline significantly in the heart failure and hospitalised groups up until the fourth minute. More recently, a prospective study of 208 older patients (>65 years) referred to a falls clinic, reviewed the 10-minute, continuous, supine BP prior to orthostatic challenge. BP and BP variability ceased changing significantly within 4 minutes, in those with OH and those without⁹. This study was based in a tertiary setting with all participants being referred for falls, syncope or dizziness with age and comorbidity contributing to a rather heterogeneous cohort.

Looking further afield, to other situations that require a stable BP reading, a similar duration of rest has been demonstrated. In 63 patients with hypertension attending a specialist clinic (73% on treatment, 78% with end-organ damage, 63±11 years), BP was determined using an automated device, every minute for four minutes in the sitting position. Blood pressure declined significantly up until the fourth reading, where there was no significant change from the previous¹⁰. Although the population are at risk of OH, it was a rather specific population in a specialist hypertension clinic, where diagnosing OH was not an outcome. Results using a similar methodology but involving 60 young, healthy, males (aged <32) found that BP became stable after 6.5 minutes on checking it with an automated device every 90 seconds. Of course, this would not be the usual population in which a postural challenge is targeted¹¹.

Although these studies are generally small and of limited methodological value, the results are consistent and in keeping with expert opinion and several international guidelines. Although it is uncertain whether the BP device used influences the baseline BP, the ideal time to measure the baseline value would be when BP is at its least variable. Variability, measured using beat-to-beat BP is at its lowest at 5 minutes, and would therefore appear to be an appropriate timing, regardless of the BP device used.

Achieving orthostasis

The objective of an orthostatic challenge is to test the integrity of the neuro-cardiovascular systems, which would ordinarily maintain a relatively constant BP¹². This challenge should be able to elicit a reduction in BP following a change in posture to the upright position. The different methods of achieving orthostasis are displayed in Figure 1, with a brief, narrative description of their advantages and disadvantages.

The lack of a recognised gold standard has limited progress with respect to assessing sensitivity and specificity of the different approaches. The majority of academic studies use either the active stand or the tilt-table test, with both of these methods also featuring in clinical guidelines (Table 2).

Sitting to standing

A recent study, which involved 326 community-dwelling older people (aged >65 years), compared the rate of diagnosis of OH using the tilt-table with continuous

BP monitoring with the sit-to-stand test using intermittent BP measurement.

The prevalence of OH using continuous BP recording and the tilt-test was much higher than the sit-to-stand test using intermittent measurement (59% and 17% respectively). This may be unsurprising given the nature of continuous BP monitoring which provides continuous BP values, in contrast to intermittent measurement which, in theory, may miss a drop in BP between recordings. For this reason, the methods used rather preclude a direct comparison between the tests. Researchers were not blinded to the tests used, different baseline rest durations were used and the duration of the orthostasis was different between the two methods. Unfortunately this study is unable to conclude whether it is the methods used to create orthostasis, the methods used to measure it or a combination of both which results in a higher diagnostic rate with one method over the other. In addition, with no longitudinal data it is unknown whether the clinical consequences of one method over the other would be significant ¹³.

Active sitting

Information about the active sit method is scarce. In a poorly described series of 98 hospitalised older patients (aged >65), who were acutely unwell and had been in bed for at least 12 hours, the prevalence of 'sitting OH' was found to be 54%¹⁴. However, it is not clear whether the patients were sitting up in bed, sitting on the edge of the bed or had moved into a chair. This has implications as sitting upright in bed causes isometric muscle contraction of the abdominal wall and thigh that can increase BP^{15 16}. In addition, it is also unknown whether the same cut-off criteria for the degree of BP drop are appropriate for the active sit test.

The active sit test has also been evaluated in a cohort of stroke patients. Forty-nine people who were living in the community and were able to walk at least 5 metres had their BP measured, first while supine and then once they had sat up. This method found the prevalence of OH to be 14% ¹⁷. However, the participants did not undergo any further testing to review the diagnosis so the sensitivity and specificity cannot be calculated.

Squatting to standing

Data regarding the squat-to-stand is limited to young, healthy individuals and not available for the investigation of OH. It is largely felt to be impractical, being suitable only for those with a good degree of strength and flexibility in the legs. As such it does not feature in diagnostic guidelines. However, in comparison to sitting-to-standing it can elicit a more profound drop in BP, but this may be exaggerated because the action of squatting causes an increase in BP, thereby raising the baseline BP ¹⁸.

Tilt-table testing

The tilt-test is felt to be an inappropriate test for initial OH as the sudden drop in BP may not be elicited, although this is based on little evidence, and should be considered as a best practice point ¹⁹. However, the tilt-test features commonly in international guidelines regarding the diagnosis of 'classical' OH.

One direct comparison of the tilt-test with the Schellong test (a 10-minute active stand) failed to capture any diagnostic difference due to the low prevalence of

OH detected in their cohort of 67 young, healthy individuals ²⁰. Conversely, in a study of 51 children and adolescents who completed a 7-minute active stand and a 7-minute tilt-test, the prevalence of syncope was significantly higher during the active standing ²¹. Similarly, a comparison of active standing and the tilt-test in seven healthy young (<40 years) individuals found a significantly greater drop in BP within the initial 30 seconds of upright posture during the active standing than with the tilt-test ²².

Looking at a population with suspected OH, 230 cases referred to a specialist clinic underwent a 45-minute tilt-test followed by a 5-minute active stand, with a 10-minute rest period between. OH was diagnosed if the BP drop lasted three-minutes or longer, which suggests the cases included were of the dysautonomic type. Comparing the data from the first five-minutes of the tests, 57% (*n* 41/72) of cases were identified in both tests, 26% were identified on active stand alone and 17% identified on tilt-test alone. Once again, when OH was identified on both the tests, the BP drop was significantly greater during the active stand ²³.

Without good quality head-to-head testing it is not possible to make evidence-based recommendations. However, international guidelines recommend the use of either the active stand or the tilt-table to achieve orthostasis. The active stand has the advantage of reflecting normal physiological responses and may be more likely to identify initial OH.

Duration of orthostasis

Generally, most protocols refer to the recommendations made by the guidelines in Table 2. These favour a three-minute upright posture in which to detect hypotension. However, the evidence is not clear-cut, with some studies suggesting the duration should be much longer in order to identify cases of delayed OH and other studies demonstrating a shorter duration being able to detect nearly all cases of OH.

In the aforementioned retrospective review of 230 cases of suspected OH, the timing of the BP drop was noted during the 45-minute tilt-test. One hundred and eight (47%) were found to have OH during the 45-minute tilt-test. Only 46% had OH within the first three minutes. A further three per cent demonstrated OH within five-minutes and a further 12% within the first 10-minutes. The remaining 39% of cases did not demonstrate OH until after 10-minutes. Of note, the authors required the BP drop to last three-minutes or longer for a diagnosis of OH, which may have excluded many cases. The use of an intermittent, automated BP device which recorded BP at one-minute intervals may have contributed to a higher level of false negatives, in what is a relatively low diagnosis rate for a cohort referred for suspected OH ²³.

In stark contrast to the study described above, a retrospective review of 66 cases of known OH in an autonomic clinic in the US, suggests a much shorter duration is required. During a five-minute tilt-test with continuous BP monitoring, 88% of the known cases of OH met diagnostic criteria with the first minute of test-testing, with 99% being diagnosed within two-minutes and the final case within

three minutes ²⁴. In this retrospective review the tilt-tests were limited to 5-minutes and may therefore have missed further cases of delayed OH.

Despite the results of these studies the consensus is to remain upright for three-minutes. However, a clinical history should be used to judge whether it is necessary to extend this duration if delayed OH is suspected. There is no data available to suggest that the duration of orthostasis should differ according to the measurement technique used, whether it be with a continuous or intermittent BP device.

Degree of BP drop

Before consensus there were several different diagnostic criteria requiring varying degrees of BP drop, typically 20-30 mm Hg systolic and/or a 10-30 mm Hg diastolic. To address this uncertainty, a study to determine the normal cardiovascular response to standing was performed in 1988 ²⁵. This study enrolled 98 healthy, hospital workers and measured their BP during using a sphygmomanometer. Subjects rested supine for three to four minutes and then stood upright for three to four minutes, during which they had two BP measurements taken. The mean systolic BP drop was 6.5 mm Hg, with 95% limits of -19 to +11. The mean diastolic drop was +5.6 (95% limits -9 to +22). It is believed that it is these two sets of confidence limits that largely informed the consensus criteria, perhaps supported by other small studies ^{26 27}. In addition, the lower 95% limit for the upright systolic BP was 92, which may have been the

supporting evidence to support the 2001 European Society of Cardiology Taskforce on Syncope diagnostic criteria (Table 2).

Interestingly, more methodologically sound evidence has recently been reported which supports the current diagnostic criteria. In 4475 adults aged over 50 years (mean age 62.8), taking part in The Irish Longitudinal Study on Ageing, an active stand was performed with continuous BP measurement. From this large cohort the authors provide normative data for each decade of life over the age of 50, during two-minutes of standing ²⁸. The normograms demonstrate a wide degree of spread in what would be considered a normal standing response. However, by providing the percentiles for the changes in BP on standing the authors demonstrate that five per cent of men and 10% of women aged 50-59 show a sustained postural BP drop below 20 mm Hg systolic or 10 mm Hg diastolic. This proportion increases with age such that between 10-25% of people have a systolic BP drop sustained below 20 mm Hg over the age of 80 ²⁸.

An update to the consensus statement in 2011 included an additional criterion for the diagnosis of initial OH. This requires a transient BP drop of 40/20 mmHg within the first 15 seconds of standing and would therefore only be diagnosed on continuous BP measurement. However, this criterion may be too lenient. In the TILDA study, 10-25% of women aged 50-59 would meet this diagnostic criteria, over 50% of women aged 60-80 and between 50-75% of women aged over 80 would be diagnosed with initial OH. A condition about which, we know very little of the natural history²⁸.

Frequency of measurement

Before the advent of continuous, non-invasive BP monitoring the frequency of BP measurement was limited to the ability of the person performing sphygmomanometry or the speed of an automated device. However, there was a lack of consensus about when to first measure the initial orthostatic BP and how often thereafter during the upright position²⁹. Further doubt arose when it became possible to record upright BP continuously³⁰.

In a recent study of 326 community dwelling older people (aged >65), using continuous BP recording and a tilt-table to diagnose OH, the prevalence was found to be as high as 59% using the raw data alone¹³. This is 10 times greater than previous estimates of prevalence using intermittent BP measurements³¹. When the raw data was transformed into 5 second averages the prevalence decreased to 52%. It is not surprising that continuous BP measurement identifies more drops in BP, but it is not known what proportion of these are artefact nor whether it improves clinical diagnosis. Indeed, the potential for a high rate of false positives has been demonstrated in a study of fifteen young, healthy adults with no postural symptoms (mean age 30 years)³². Five of the participants demonstrated a diagnostic postural drop in BP in the initial stages of standing. However, this small study was performed before the update in consensus criteria and it is unknown whether any of the participants would have met the criteria for initial OH, which requires a more profound drop in BP.

When using intermittent measurement, evidence suggests the first measurement should be taken within the first minute and preferably within the first 30 seconds. In a study of 23 older people at a geriatric medicine unit (mean age 81 years), an orthostatic BP was measured during an active stand. BP was measured using intermittent sphygmomanometry at 30 seconds, 60 seconds and every minute thereafter for 5 minutes, the nadir BP drop was found at 30 seconds ³³. Similarly, a study of 110 people with OH, who had continuous BP measurement recorded during a tilt-test, found that the majority of cases reached a nadir BP within the first 60 seconds (although the interquartile range was wide 12-62 seconds) ³⁴. This is further supported by the findings of the TILDA study (described above) which demonstrated the greatest BP drop within 30 seconds of standing upright ²⁸.

If continuous BP monitoring is not available, there are limited data suggesting that an automated BP device is slightly more sensitive and specific than using a sphygmomanometer. The authors of this study assumed that continuous monitoring is the gold standard and found that intermittent measurement missed the majority of cases of OH (automated device sensitivity 37%, specificity 92%. Sphygmomanometer sensitivity 25%, specificity 90%) ³⁰.

These data suggest that when using an intermittent device it would be ideal to measure the BP at or around 30 seconds, the commonest timing for the BP nadir. With the results from the TILDA study (see Table 1) it would then be useful to record the BP at or around 30 seconds later, if practically feasible. Thereafter, there is little evidence to guide frequency of measurement but it may be

considered good practice to measure BP at 60 second intervals with the final measurement at 3 minutes.

Reproducibility

Reproducibility of an orthostatic BP profile is very poor, regardless of the methods used to measure it. The presumption is that there are several confounding factors including diurnal variation, presence of vaso-active hormones, plasma volume, cognitive activity and vaso-active medication³⁵. But even when carefully controlling for these conditions the reproducibility remains poor, as described below.

In those with autonomic failure, the reproducibility is greater, with 79% of cases with neurogenic OH eliciting a diagnostic drop on two separate visits. In the same study, this compared to a reproducibility of 67.5% in all cases of OH tested on two separate occasions, controlling for diurnal variation. In this study, a subgroup of 10 cases returned for an active stand in the afternoon. The degree of the postural BP drop was significantly lower than when performed in the morning but the effects of this on diagnosis is not reported ³⁶.

Reproducibility has been shown to be even poorer in the ward-based setting. A study of 502 patients admitted consecutively to an acute inpatient geriatric ward, had an active stand performed 30 minutes after breakfast, lunch and dinner. Following breakfast, OH was present in 39% of patients, with a smaller BP drop in a further 19% of cases (10-19 mmHg). Only 70% of those with OH in

the morning were found to have OH later in the day whereas 57% of those with a smaller BP drop met the diagnostic criteria later in the day. Furthermore, for those with no BP drop, or only a mild drop (<10 mm Hg), 40% and 48% went on to demonstrate OH in the afternoon. This study is limited by the effects of meals, timing of medication, a heterogeneous group of acutely unwell people and the effects of multiple investigators measuring BP ³⁷. However, these limitations reflect real circumstances on the majority of wards. Similar results have also been found in the care home setting, with diagnosis rates of OH declining when measured over the course of a day (kappa 0.12-0.47 for agreement), but with slightly better agreement between active stands when performed at the same time on different days (kappa 0.17-0.32 for agreement), supporting that diurnal variation is a problem ³⁸.

In the primary care setting, reproducibility is similarly poor. A large population study of BP in Italy, involving 444 GP practices performed an active stand in 3858 people and repeated it 7 days later. Although the overall prevalence of OH remained reasonable consistent, 13.8% and 12.6%, the intra-individual reproducibility was poor with only 36% of cases being identified on both visits. However this study is very much limited by the number of different investigators performing the active stand, opening the study to huge heterogeneity in measurement technique ³⁹.

The findings of these studies add little evidence to support a recommendation for the optimum timing of performing an orthostatic challenge. Expert commentaries on OH have described the theoretical advantage of investigating

OH in the morning⁴⁰. Following a period of nocturnal supine rest the perfusion pressure of the glomeruli is increased such that there will be an increased diuresis, particularly in older people whose response to vasopressin is attenuated, leading to a reduced plasma volume ⁴¹. In theory, this creates a greater challenge to the neuro-cardiovascular homeostatic mechanisms thereby revealing an underlying deficit. A similar exaggerated challenge to the homeostatic mechanisms would be to perform orthostasis following ingestion of a carbohydrate load, which leads to theoretical increase in the splanchnic-mesenteric venous capacitance, in effect reducing effective circulating volume ³⁵. However, in the absence of quality data there remains much uncertainty, in particular regarding diagnostic accuracy and false positive results.

Symptoms

The relevance of asymptomatic OH is unknown. Consensus guidelines advise that a diagnosis of OH can be made in the absence of symptoms. If this is the case then asymptomatic OH may only be identified in at risk populations or during screening programmes, otherwise the reason for performing an orthostatic challenge is not clear. Estimates of asymptomatic OH may be artificially high due to the non-specific nature of symptoms. Indeed, non-specific symptoms such as weakness and fatigue, loss of concentration, blurred vision and nausea are all common (up to 72% of cases of OH) and may not be considered as symptoms when performing an orthostatic challenge ⁴². For those cases that truly are asymptomatic there is no existing evidence regarding the natural history and clinical outcomes, nor whether treating it is of any benefit.

Discussion

The diagnostic criteria for OH are not well evidence-based, and are largely informed by small studies of limited quality, expert opinion and consensus. Indeed, during this review of the literature, it became apparent that there are no studies reporting on the diagnosis of OH using internationally recognised reporting standards such as STARD (Standards for Reporting of Diagnostic Accuracy Studies)⁵. This is surprising given the high prevalence of OH in a rapidly expanding older population. The principle limiting-factor appears to be the lack of an agreed gold standard, to which studies of accuracy can be compared. Without this it will be challenging to conduct rigorous studies and develop a robust, evidence-based investigation.

One of the limitations facing the diagnosis of OH has been the advance of technology, which has become widely accepted and adopted before the existence of an evidence base. The advent and increased use of non-invasive, continuous BP monitoring which is capable of detecting transient drops in BP which would not be observed using intermittent sphygmomanometry is the best example. The significance of these short-lived drops, which meet the diagnostic threshold, is not known. For this reason, the updated consensus criteria in 2011 added the word *sustained* to their diagnostic criterion. There is however, little to no evidence to inform what duration of BP drop should be considered as *sustained*. Similarly, the advances in technology led to the recognition of a new sub-type of OH, initial OH. This is unlikely to be identified using intermittent BP

measurement and it is recommended to use continuous monitoring if it is suspected, as the initial drop in BP typically recovers well within the first 30 seconds of standing upright ¹⁹.

Without a consensus on which diagnostic approach should be considered the gold standard, further progress is perhaps limited. However, in order to support one method over another what are currently needed are longitudinal studies to identify the clinical significance of the different diagnostic patterns. For example, are transient BP drops part of the natural history, or a precursor to sustained OH? Does the treatment of initial OH result in improved clinical outcomes?

One of the difficulties limiting the comparison of different diagnostic approaches is the poor reproducibility, even when using the same equipment. This really limits the ability to accurately compare sensitivity and specificity. It also limits diagnosis, assessing response to treatment and defining the natural history of the condition. To improve reproducibility it would appear that aiming to limit the effects of diurnal variation, vaso-active medication, meals and physical and mental activity on BP may be of benefit when repeating an orthostatic challenge.

With the evidence presented in this review there is an obvious lack of reference to clinical details to inform diagnosis. Given the many unanswered questions and uncertainties that exist, the findings from the clinical history and examination may help to improve the interpretation of the BP profile, particularly if the result is equivocal. This may be particularly challenging when

faced with an asymptomatic drop in BP, but without good quality longitudinal studies it remains uncertain whether treatment is beneficial.

It is anticipated that the number of 60-74 year olds will increase by 50% and the number of over 80 year olds by 100% within the next 20 years. We can therefore expect to see increasing numbers of people with OH. However, there may also be a synergistic effect as OH is found in approximately 50% of people with chronic disease⁴³. With the survival of younger people with chronic disease increasing into old age we may well see a rapidly expanding older population with an expanding proportion affected by OH. With this in mind it is imperative that we improve the diagnostic approach to people with suspected OH and address the areas of uncertainty.

Recommendations

Baseline: 5 minutes supine rest prior to checking baseline BP.

Orthostasis: An active stand or tilt-test is the preferred method, with active stand being preferable for suspected initial OH.

Duration: Two to three minutes active standing, or if delayed OH is suspected, then 10 minutes or longer on a tilt-table may be required.

BP drop: In general, use a systolic drop of 20 mm Hg as a guide and 10 mm Hg for diastolic BP. Interpret brief drops in BP alongside the clinical information.

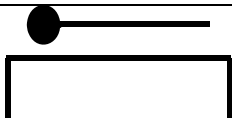

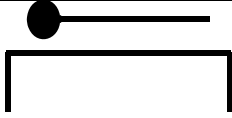
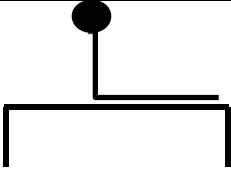




Initial OH requires a greater drop in BP within the first 15 seconds; therefore continuous monitoring will be required.

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Test	Baseline	Orthostasis	Advantage	Disadvantage
Active stand			Reflects usual physiological response to standing	May prolong time to achieve upright position
Active sit			Useful for those who are unable to stand	Isometric exercise to maintain position may increase diastolic BP. Diagnostic criteria may not be appropriate.
Sit to stand			Reflects every day activity. Simple with little assistance or equipment	Venous pooling in legs and pelvis during baseline
Squat to stand			Profound challenge to neuro-	Impractical. High rate of false



			cardiovascular system	positives.
Tilt table test			Controlled conditions and timing. Provides support for people unable to stand.	Does not replicate everyday situation. Equipment required. Not suitable for initial OH.

Figure 1. A narrative illustration and review of different approaches to performing an orthostatic challenge.

Study	Conclusion	Comments
Length of time required to achieve a stable baseline blood pressure in the diagnosis of orthostatic hypotension ⁹	There is little benefit to resting supine longer than 5 minutes prior to an orthostatic challenge.	These findings were derived from beat-to-beat BP monitoring in a heterogeneous sample of 208 individuals referred to a tertiary clinic.
The prevalence and pathological correlates of orthostatic hypotension and its subtypes when measured using beat-to-beat technology in a sample of older adults living in the community ¹³	<p>The prevalence of BP drops meeting diagnostic criteria were 59% in healthy older people.</p> <p>Three distinct patterns of BP drop were identified (small drop-fast recovery, medium drop-slow recovery, large drop-non-recovery).</p>	A large cohort (326) of healthy, older people underwent tilt-test with beat-to-beat BP monitoring. The value of the three BP profiles is not known but the authors hypothesise it may help direct therapy.
Age Related Normative Changes in Phasic Orthostatic Blood Pressure in a Large Population Study: Findings from the Irish Longitudinal Study on	An initial orthostatic BP drop is common and occurs within 30 seconds. Non-recovery of the BP drop beyond 30 seconds is abnormal and is more common with	This large and well-conducted study provides age-related normative data for orthostatic responses and confirms that a systolic drop of 20

Ageing (TILDA) ²⁸	ageing.	mmHg and diastolic drop of 10 mmHg should be considered abnormal beyond 30 seconds.
Factors affecting continuous beat-to-beat orthostatic blood pressure response in community-dwelling older adults ⁴⁴	The authors found that time of day, time since last meal meal and medication were not associated with the drop when age was taken into account.	109 community-dwelling people over 50 years old, assessed using beat-to-beat BP during active stand, during a pilot study for TILDA.

Table 1. A summary of research studies relevant to the diagnosis of orthostatic hypotension, published since the 2011 consensus criteria².

<p>1996 Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American Autonomic Society and the American Academy of Neurology ⁴</p>	<p>A reduction in systolic BP of at least 20 mm Hg or diastolic BP of at least 10 mm Hg within 3 minutes of standing.</p> <p>An acceptable alternative to standing is the demonstration of a similar drop in BP within 3 minutes, using a tilt table in the head-up position, at an angle of at least 60 degrees.</p>
<p>2001 Task force on syncope, European Society of Cardiology. Part 2. Diagnostic tests and treatment: summary of recommendations ⁴⁵</p>	<p>Orthostatic BP measurements are recommended after 5 minutes lying supine, followed by each minute, or more often, after standing for 3 minutes.</p> <p>Continue measurements for longer if BP is still falling at 3 min.</p> <p>A decrease in systolic BP ≥ 20 or a decrease to <90 mmHg is defined as OH whether or not symptoms occur.</p>
<p>2006 European Federation of Neurological Sciences guidelines on the diagnosis and management of orthostatic hypotension ⁶</p>	<p>A 5-minute supine rest is followed by 3 minutes upright on a tilt-table. It is considered positive if systolic BP falls below 20 mmHg and diastolic BP below 10 mmHg of baseline.</p>

	<p>HUT is recommend if active standing is negative and history is suggestive of OH.</p>
<p>2011 Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome ²</p>	<p>A sustained reduction of systolic BP of at least 20 mmHg or diastolic BP of 10mmHg with 3 minutes of standing or tilt-testing.</p> <p>In patients with supine hypertension, a reduction in systolic BP of 30 mm Hg may be more appropriate.</p> <p>A transient BP drop of >40 systolic BP or >20 diastolic BP within 15 seconds of standing is diagnostic of initial OH.</p> <p>Delayed OH may be revealed in patients with suspected OH by extending the duration of stand or tilt-testing.</p>
<p>2013 Evaluation and treatment of orthostatic hypotension. The American Society of Hypertension ⁴⁶</p>	<p>A 5-minute supine rest is followed by Checking the BP at 1 minute standing and 3 minutes of standing. Diagnosis is made in the presence of a reduction in systolic BP of >20 (or >30 in the presence of hypertension) or diastolic BP >10 mm Hg.</p>

	Sitting-to-standing is an alternative but less preferable.
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Table 2. The diagnostic criteria for OH from different guidelines.